

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

OXYTHIOQUINOX

SB 950-032, Tolerance # 00338
Chemical Code #: 000410

March 4, 1987

Revised 1/29/88, 8/18/88, 5/29/90, 8/16/91, 7/20/93, 10/10/95, 8/9/96

I. DATA GAP STATUS

Combined rat:	No data gap, possible adverse effect.
Chronic dog:	No data gap, possible adverse effect
Onco mouse:	No data gap, no adverse effect
Repro rat:	No data gap, possible adverse effects
Terato rat:	No data gap, possible adverse effect
Terato rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, possible adverse effect
Chromosome:	No data gap, possible adverse effect

DNA damage: No data gap, no adverse effect

Neurotox: Not required at this time

-----**Note, Toxicology**
one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

File name: T960809

Toxicology Summary updated by T. Kellner, 8/16/91, 7/20/93; by H. Green & M. Silva, 10/10/95;
by Gee, 8/9/96.

Reconciled with library printout dated 11/3/93 (through record #126846, volume 338-103).

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

**** 102 126440**, "Technical Grade Oxythioquinox (MORESTAN*): A Combined Chronic Toxicity/Oncogenicity Feeding Study in the Fischer 344 Rat", (W. R. Christenson and B. S. Wahle, Miles, Inc., Agriculture Division, Toxicology, 17745 South Metcalf, Stilwell, KS. 66085-9104, Report # 106333, 9/23/93). Morestan* technical (oxythioquinox; 93.56 % pure) was fed in diet to Fischer CDF(F-344)/BR rats (60-70/sex/dose) at 0 (acetone/corn oil and Purina Mills Rodent Lab Chow 5001-4), 40, 150, and 560 ppm in the diet for 2 years. Ten (low and mid dose) to 20 (control and high dose) rats/sex/dose were sacrificed at 1 year. Chronic NOEL = 150 ppm (Body weights were significantly decreased in both sexes, primarily at 560 ppm. An increased incidence in broken teeth in both sexes was observed at 560 ppm. There was decreased Hb, Hct, MCV, MCH, MCHC and increased platelets in both sexes, primarily at 560 ppm throughout the study. Clinical chemistry showed increased phosphate and calcium in both sexes at \geq 150 ppm. Absolute and relative adrenal, kidney and liver weights were increased in both sexes at 560 ppm. Increased histopathology in liver (cystic degeneration, angiectasis, eosinophilic foci, hepatocellular focal hyperplasia), kidney (tubular hyperplasia), skeletal muscle (atrophy), testes (degeneration, tubular mineralization) and epididymides (abnormal spermatozoa, aspermia) were observed primarily at \geq 150 ppm.) **Possible adverse effect:** Oncogenic NOEL = 40 ppm (Increased combined neoplasms (adenoma, adenocarcinoma, undifferentiated carcinoma) of kidney tubular epithelium occurred at \geq 150 ppm. **Acceptable.** (Green & Silva, 10/4/95)

100 124985 This volume contains an adverse effects disclosure for the definitive combined rat study (DPR volume/record #: **338-102/126440**). No worksheet. M. Silva, 10/5/95.

023 946716 "Studies of Chronic Toxicity to Rats." (Bayer, Institute fur Toxikologie, 8/30/66, Report No. 18795) Oxythioquinox, Bayer 36 205, 91% Morestan; fed for 2 years to 50 "random breed" rats/sex/test group and 100/sex for controls, at 0, 10, 25, 60, 150 or 500 ppm; no effect on food consumption in males but reduced intake in females at 500 ppm; yellow discoloration of fur in 500 ppm and later in 150 ppm groups; reduced weight gain in both sexes in high dose group; no effect of treatment on survival; major cause of interim deaths was pneumonia; **possible adverse effect:** increase in average liver organ weight in all treatment groups in both sexes with approximately the same extent in all groups; no effect on minimal hematological parameters after 2 years (only analysis); NOEL = 150 ppm (liver pathology - vacuolar cytoplasm swelling, necrosis, bile duct hyperplasia at 500 ppm, reduction in spermatogenesis); no evidence for oncogenicity; while there was an apparent increase in the incidence of reduction in spermatogenesis at 150 ppm (5/13 at 150 versus 7/31 in control), the incidence was not statistically significant by Fisher's exact test while the incidence at 500 ppm (13/17) was highly significant; UNACCEPTABLE (no individual data except for cause of death and tumor analysis, no analysis of diet, no individual body weights, food consumption, clinical observations). JR(G), 3/7/85
EPA 1-liner: No CORE grade. NOEL = 60 ppm (coat discoloration, vacuolar cytoplasm swelling, reduced spermatogenesis.)

023 946717 Histopathology report for 946716.

023 946718 Organ weight data for 946716.

028 016823 Appears to be individual organ weights and hematology values for 946716. Bayer report #21884, 8/2/66.

028 016826 "Chronic Toxicological Studies on Rats (Two-year Feeding Experiment)." (Bayer AG, Institut fur Toxikologie, 8/3/71, Report No. 35077 or No. 3684), Bayer 36 205, technical grade, no purity stated; fed in the diet for 2 years at 0, 3, 6 or 12 ppm as a follow-up study to the earlier one, #946716; 30 Wistar rats/sex/test group, 60/sex in controls; no differences in food consumption, body weight gain, hematology parameters, mortality,

urinalysis, liver function tests were reported; no histopathological changes due to test article reported; NOEL > 12 ppm; UNACCEPTABLE (inadequate number of animals, no analysis of diet, no toxicity at high dose.) JR(G), 3/7/85.
EPA 1-liner: Supplementary. Oncogenic NOEL > 12 ppm (HDT), systemic NOEL = 12 ppm (HDT).

028 017330 "Report on Studies with Morestan for Toxic Effects on Liver." (Bayer AG, no date, Report No. 028572) Morestan, no purity stated; fed at 0, 10, 25, 60, 150 or 500 ppm to 10 males and 20 females per group; after 70 days, 8 males and 16 females were mated; males were infertile at 500 ppm (not clear if this is part of #946721); animals were sacrificed at 7 months (high dose) or 8 and 9 months (remainder); liver weights determined and examined macroscopically - no findings reported; of 24 livers from high dose group, 14 showed toxic injury, 2 were questionable and 8 lacked any indication; UNACCEPTABLE (incomplete study and report). Possible **adverse effect**: liver changes. NOEL = 150 ppm. JR(G), 3/7/85.

EPA 1-liner: No CORE grade. Reproductive NOEL = 60 ppm (decreased pregnancy rates, decreased litter size, fetotoxic NOEL = 60 ppm (increased pup mortality), liver pathology NOEL = 150 ppm. See under Reproduction, Rodent, #946721, -22.

Letter dated 10/30/92. (No document or record number). Reports interim findings from the definitive rat chronic/oncogenicity study (100-126440), reviewed above. High-dose (560 ppm) Fischer 344 males had an increased incidence of testicular tubular degeneration at the one-year sacrifice. As much as 30% of the tubule cross sections were reported to be degenerated with loss of mature spermatozoa and loss of most of the germinal cells preceding the spermatids in development. This finding was reported previously in Miles report 18795 and 18796 (-023:946716, see above). No data were provided in the letter. No Worksheet. 7/19/93.

CHRONIC, DOG

023 946714, "Chronic Oral Toxicity of Morestan (Bayer 36205) to Male and Female Dogs." (U. of Chicago for Bayer, 5/28/66, Report No. 18290) Bayer 36205, technical, 91%, fed for 28 months to Beagle dogs at 0, 10, 25 or 50 ppm, 2/sex/dose; diets prepared biweekly; no effect

on growth rate at any dose; no effect on food intake; no effects due to the test article were reported; UNACCEPTABLE (inadequate number of dogs, no evidence of toxicity to justify high dose, summary data only) JR(G), 3/6/85
EPA 1-liner: Supplementary. NOEL = 50 ppm (HDT).

****026 016818**, "Chronic Dietary Toxicity of Oxythioquinox (Morestan) to Dogs, Study No. 80-174-02." (Mobay, Environmental Health Research, 3/7/83, #82654, Toxicology Report No. 363) Oxythioquinox, technical, 95.8%, Batch No. 9030173; fed in the diet for 1 year at 0, 25, 75 or 225 ppm; diet analysis performed monthly; blood chemistry, hematology and urinalysis at initiation, 2 months and termination; NOEL = 25 ppm (microscopic liver changes - at 225 ppm, "...hepatic change was that of a marked hepatopathy with early cirrhosis.") Also, blood chemistry elevations of serum alkaline phosphatase and SGPT were added evidence of liver changes. Three collections of semen from dogs fed up to 225 ppm showed no reduction in quantity or quality; Food consumption was decreased in males later in the study at 225 ppm but unaffected in females; ACCEPTABLE with **possible adverse effect** to the liver (also a target organ in the rat). The initial review, JR, 3/7/85, indicated justification of dose selection was needed. The adequacy of the dose is justified in a letter dated 11/26/86, in Document 3338-047, based on the liver pathology, as indicated above. JR(G), 3/7/85 and 3/2/87.

092 114868. Addendum to 026 016818. Micropathological historical control data supporting a NOEL of 25 ppm in the liver was provided by Miles, Inc. in response to a U.S. EPA review of the chronic dog study. No worksheet. 7/19/93.

ONCOGENICITY, RAT

026 016824 "Final Report on Carcinogenic Study with Morestan Active Ingredient (= BAY 36 205)." (Bayer AG, Institut fur exp. Pathologie, 8/70, Pharma Report No. 2211, also 28570.) BAY 36 205, 92.4%, Batch 314; fed to 25/sex/group; total dose of 16.7 g/kg in daily doses of 22.5 - 180 mg/kg; UNACCEPTABLE (single dose, unclear protocol for dosing, controls given saline by subcutaneous injection, inadequate number of animals at risk). No evidence of oncogenicity induced by Bayer 36 205 is reported. JR(G), 3/8/85.
EPA 1-liner: Supplementary. Negative carcinogen.

ONCOGENICITY, MOUSE

** 057, 059, 064 068593, 070809, 075753 "Carcinogenicity Study on NMRI Mice (21-Month Administration in the Feed)," (Kroetlinger, F. & Janda, B., Bayer AG, FRG, June 1983, Study T 5010716, Mobay No. 96755 and 96755-1), Oxythioquinox technical (SAS 2074, 95.2%, Batch 9030173) was fed in the diet at 0 (vehicle = DAB8 peanut oil), 90, 270 or 800 ppm to Bor:NMRI mice (70/sex/group with 20/sex/group) for 12 months. No evidence for an oncogenic effect was observed. NOEL (males) = 270 ppm, NOEL (females) = 90 ppm (body weight gain was decreased in high dose males; survival was decreased in mid- and high-dose females; an increase in spleen weights in females at all doses at 12 and 21 months sacrifice was observed and there was evidence of extramedullary hematopoiesis especially in females. Review by Gee, 8/18/88.) Volume/record #'s: 064/075753 contained a GLP statement and an addendum to the original report; 059/070809 contained information regarding the number of days on test occurred for each animal of all dose groups. ACCEPTABLE. M. Silva, 5/25/90.

081 098391. Addendum for 057, 059, 064 068593, 070809, 075753. Volume contains historical control data from 23 studies concerning the frequency of lung adenomas and carcinomas, study duration, animal husbandry and identification of pathologists. No worksheet. 7/19/93.

055 70384 Duplicate of Mobay No. 96755 shown above.

096 122335 Addendum for 057, 059, 064 068593, 070809, 075753. Volume was provided by Miles, Inc. in response to the Health and Welfare Department of Canada request for the following information: a) Duration of the acclimatization period. b) Individual animal data on mortality. c) Individual animal data on food consumption; and d) Definitions of the codes listed in the pathology report. No Worksheet. 7/19/93.

109 146218 Supplement for 057, 059, 064, records 068593, 070809 and 075753. The document, Bayer 96755-1, consists of historical control data for lung adenomas and carcinomas, requested by US EPA in their review. This may be a duplicate of 081 098391 [unable to locate that volume, 8/8/96] The initial study was reevaluated by Medical Toxicology as acceptable and no

adverse effect was identified on 5/25/90. No change in status with the submission of 146218.
No worksheet. Gee, 8/8/96.

REPRODUCTION, RODENT

023 946721, 946722, "Rat Breeding test." (Bayer, Inst. fur Toxikol., Report no. 18794, 8/4/66) Morestan, 91%, Batch 124; fed in the diet to 8 males and 16 females per group at 0, 10, 25, 60, 150 or 500 ppm; 3 generations, 2 litters each; necropsy on F3b pups only; reduced food intake and weight gain in F0 at 500 ppm; zero pregnancies at 500 ppm - further testing indicated the lack of fertility was due to males; pregnancy rate at 150 ppm was reduced slightly for F1a with less effect for F1b litters; pregnancy rate in the F2a and F2b matings were comparable, including 150 ppm group. **Possible adverse effects:** reduced fertility, litter size, and postnatal survival. Repro NOEL = 60 ppm (decreased pregnancy rate, decreased litter size). sys NOEL = 150 ppm (reduced weight gain); UNACCEPTABLE (no individual animal data, no necropsy on parental animals, no analysis of diet.) Testes weights for 3-week old pups only so no information of adult males after exposure for 100 days. JR(G), 3/7/85

**** 037 027104**, "SS 2074 (New Designation SAS 2074) Two-generation Study with Rats." (Bayer AG, Institute of Toxicology, 7/6/84, Report No. 12794, also 88502) SS 2074, chinomethionate, batch no. 9030173, 94.6%; fed in the diet to 10 males/20 females per group at 0, 15, 60 or 240 ppm, two generations, two litters per generation; dose selection based on pilot study - data not included; necropsy on F2b pups and F1b parents; yellow coat at 240 ppm; slower body weight gain in 60 and 240 ppm groups; fertility rates comparable. **Adverse effect:** litter size and viability at 5 days slightly decreased in some litters at 240 ppm. Pup birth weights comparable; sys NOEL = 60 ppm (body weight gain), reproductive NOEL = 60 ppm (decreased litter size and viability). The difference in weight gain was marginal and more pronounced in females than males. No significant difference in testes weights in F1b adult males. ACCEPTABLE. Originally reviewed as unacceptable based on the number of males per group. Reconsideration indicates that, since two litters and two generations were available

for evaluation for effect, in addition to an earlier study, #946721, collectively, sufficient data are available.
JR(G), 9/6/85 and 3/3/87

REPRODUCTION, SUPPLEMENTAL

024, 031 016820, "Evaluation of the Effects of Oxythioquinox on the Semen Quality in Canines (Includes Technical Operating Procedure)".

TERATOLOGY, RAT

028 016825, "Studies on Rats for Embryotoxic and Teratogenic Effects." (Bayer, Institut for Toxikologie, 11/16/70, Report No. 29036) Bayer 36 205, technical, 91%, Batch 124; fed in the diet at 0, 100, 250 or 750 ppm. days 1 - 20, to 9 - 11 rats per group; maternal NOEL = 100 ppm (marginal effects at 250 ppm, decreased weight gain, food intake); developmental NOEL = 250 ppm (decreased fetal weight, complete resorptions in 8/9 pregnant females in the presence of marked maternal toxicity in terms of significant reduction in food intake and clinical observations - stated to sit in one corner of the cage, have ruffled fur and eat poorly); no evidence for malformations; UNACCEPTABLE (inadequate number of females at risk, no analysis of diet - not the best route of administration.) JR(G), 3/7/85

EPA 1-liner: CORE grade minimum. Teratogenic NOEL > 750 ppm (HLT), fetotoxic NOEL = 250 ppm (decreased fetal weight and growth), reproductive NOEL = 250 ppm (increased resorptions), maternal NOEL = 100 ppm (ruffled fur, poor food consumption.)

043 047537, "Teratology Study in Rats." (IRDC, draft report, 8/15/86 - see 053 for final report)

****053 063869, 061042**, "Teratology Study with Morestan in Rats." (IRDC, 6/3/87, Mobay Report 93098 and supplement), Oxythioquinox, technical, 94.4%; given by oral gavage to 25 females at 0 (0.5% methylcellulose), 10, 30 or 90 mg/kg, days 6 - 15 of gestation; maternal NOEL = 30

mg/kg/day (decreased body weight and weight gain, decreased food intake), developmental NOEL = 30 mg/kg/day (increased postimplantation loss, malformations such as omphalocele, microstomia, skeletal malformations); because results were not clear concerning the fetal malformations at 90 mg/kg/day in this study, a second teratology study was conducted - see Record # 063870; **possible adverse developmental effect**; ACCEPTABLE. Gee, 1/29/88.

084 111304 Addendum to 053 063869, 061042. Historical control data regarding the incidence of spontaneous cleft plate, micronathia, anasarca and malformed limb bones. No worksheet. 7/19/93.

**** 053, 103 063870, 061053, 126846** "Teratology Study in Rats". (International Research and Development Corporation, 8/14/87, Mobay report No. 94848) Oxythioquinox technical, 94.4%; given by oral gavage at 0, 50, 75, 90 or 110 mg/kg/day, days 6 - 15 of gestation, 25 per group; maternal NOEL = 90 mg/kg/day (equivocal decrease in body weight gain and food intake), developmental toxicity NOEL = 50 mg/kg/day (increased postimplantation loss, malformations); **possible adverse developmental effect** - see also record # 063869, 061042; acceptable. (Gee, 1/29/88). Supplemental data (DPR volume/record #: 338-103/126846) were historical controls. Silva, 10/6/95.

TERATOLOGY, RABBIT

****032 016819**, "Ss 2074 (Morestan Active Ingredient) Evaluation for Embryotoxic and Teratogenic Effects in Orally Dosed Rabbits." (Bayer AG, Institut fur Toxikologie, 2/5/81, Report No. 9784, also 69379), Ss 2074, 91.5% given by oral gavage to 15 Himalayan rabbits per group at 0 (0.5% Cremophor), 10, 30 or 100 mg/kg, days 6 - 18; ACCEPTABLE with no adverse teratogenic effect reported. Nominal NOEL = 10 mg/kg (decreased placental weight at 30 mg/kg, maternal effects at 100 mg/kg). JR(G), 3/8/85. No EPA 1-liner available.

091 114819, " A Developmental Toxicity Study with Morestan Technical in Rabbits", (G.R. Clemens & R.E. Hartnagel Jr., Miles Inc., MTD0253, Report No. 102682, 5/19/92). Oxythioquinox (purity 94.2%, batch 203 930 103) was administered by oral gavage at concentrations of 0 (CMC), 3, 12, or 50 mg/kg to twenty artificially inseminated New Zealand White Rabbit does/group during gestation days 6 through 18. Maternal NOEL = 12 mg/kg/day (reduced weight gain, food consumption and stools in the 50 mg/kg group). **No Adverse Developmental Effects. Developmental NOEL = 12 mg/kg/day (increased abortion and percent pre-implantation loss and decreased litter size and implantations per litter in the 50 mg/kg group) ACCEPTABLE. Kishiyama, Kellner and Gee, 7/15/93.

MUTAGENICITY, GNMU

Bacterial systems

032 016816, "Report of Mutagenicity Test on Bacteria." (Nitokuno, 11/5/75) Morestan one of a series of compounds tested with and without rat liver activation with Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100, 10 to 1000 ug/plate. No data except "-" reported for all strains with and without activation. JR(G), 3/8/85

038 036706, "Ames Test for Morestan (Chinomethionat)." (Mobay, 10/27/77, Report No. 89029) Morestan, lot 7/23/74, 89.6 - 89.8%; tested in Salmonella strains TA1537, TA98 and TA100, with and without rat liver activation, at 3.15, 10, 31.5, 100 or 315 ug/plate, duplicate plates, single trial; no increase in reversion rated; notation of precipitation at all concentrations; plate incorporation method; no data for TA98 are included; UNACCEPTABLE (not all strains tested.) JR(G), 12/27/85.

038 036707 "Chinomethionat (Morestan) Mutagenicity Test on Bacterial Systems." (Institute of Environmental Toxicology, 11/26/79, Report No. 89030) Chinomethionat, 91%; tested in Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100, with and without rat liver activation; also E. coli strain WP2tested at 0, 1, 5, 10, 50, 100, 500, 1000 and 5000

ug/plate, in duplicate; no comment on solubility (see 36706); no increase in reversion rate; cytotoxicity at ≥ 500 ug/plate; UNACCEPTABLE (duplicate plates only). JR(G), 12/27/85 and 8/18/88.

Mammalian systems

047 50391, "CHO/HGPRT Mutation Assay in the Presence and Absence of Exogenous Metabolic Activation." (Microbiological Associates, 11/26/86, Study No. T4284.332, Tox. Report No. 772) Oxythioquinox, 94.4%, lot 9030173; tested with activation at 0, 0.1, 0.5, 1.0, 3.0 and 5.0 ug/ml and without activation at 0, 0.1, 0.5, 1.0, 1.5 and 2.0 ug/ml, duplicate cultures which were pooled before plating 5 plates for mutants; incubated with test compound for 5 hours, 10 uM thioguanine to select; no concentration dependent increase in mutation frequency; UNACCEPTABLE (no confirming repeat trial). JR(G), 3/2/87

SUMMARY: Although all of the studies have deficiencies which make them individually inadequate, taken collectively the data are sufficient to evaluate that oxythioquinox is not mutagenic in bacteria. The single trial in mammalian cells was also negative. Gee, 3/4/87.

UPDATED SUMMARY: The most recent mutagenicity study submitted to CDPR (338-074, 096665) involved mammalian (CHO) cells that received concentrations of oxythioquinox that were higher than previous mammalian in vitro studies. An equivocal mutagenic response was indicated by this latest study. Kellner, 8/16/91.

**** 338-074 096665** Young, R. "Mutagenicity Test on Morestan Technical in the CHO/HGPRT Forward Mutation Assay with Duplicate Cultures and Independent Repeat" (Hazleton Laboratories America, Inc., Report #100289, 10/24/90). Oxythioquinox Technical (Morestan*), lot 9030173, 94.5% purity was tested in vitro for forward mutations at the HGPRT locus in Chinese hamster ovary cells with and without metabolic activation with Aroclor 1254 stimulated rat liver S-9

fraction with 2 cultures/dose at levels of 0 (control), 5, 10, 15, 20, 23, 27, 30 and 40 ug/ml without S-9 and 1, 10, 12, 14, 16, 18, 20 and 30 ug/ml with S-9 in 2 trials (second trial used modified dose ranges). Cells were exposed to test article for 4 hours. **Possible Adverse Effect:** Equivocal for mutagenicity (induction of forward mutations at the HGPRT locus) at 14 ug/ml dose without S-9. ACCEPTABLE. (Kellner and Gee, 8/7/91).

MUTAGENICITY, CHROMOSOME

**** 066 087550** "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells" (Putnam, D.L. & Morris, M.J., Microbiological Associates Inc., Mobay No. 99655, Lab. No. T8419.337026, 7-27-89). Chinese hamster ovary cells were exposed to Morestan technical, 78R-89-1, Batch No. 9030173, 94.7%, at concentrations of 0 (acetone), 0.65, 1.3, 2.5 and 5 µg/ml (no S-9) and 0, 1.3, 2.5, 5 and 10 µg/ml with S-9 from livers of Aroclor-induced male Sprague-Dawley rats. A confirmatory test with S-9 was conducted at 5.9, 7.7, 10, 13 and 17 µg/ml. Duplicate cultures were used at each treatment level. In the absence of activation, cells were exposed for 18 hours, in the presence of activation, cells were exposed for 2 hours. 100 metaphase cells per culture flask were scored and mitotic index (based on 500 cells) was calculated for each culture. **Possible adverse effects.** When S-9 was used at concentrations of ≥ 10 µg/ml strongly positive results (increased gaps, chromatid breaks and exchanges and chromosome breaks) were produced in both the initial and confirming tests. ACCEPTABLE. D. Shimer & M. Silva, 5/25/90.

025 946723, "Dominant Lethal Test on the Male Mouse to Evaluate for Mutagenic Effect." (Bayer AG, Institute of Toxicology, 6/24/80, Report No. 9263, Study No.: Ss2074/001) Oxythioquinox, 90.3%, 50 males per group given single oral dose of 0 or 750 mg/kg with dose selection based on pilot study in females with 4 per group given 1000 or 2000 mg/kg with 1000 mg/kg "...tolerated with faint symptoms." Males were mated 1:1 for four days for 12 periods; overall fertilization quotas were lower in the treatment group (see under reproduction); no evidence for a dominant lethal effect; UNACCEPTABLE (no concurrent positive control or historical data presented, single dose, unclear statement on page 9 in reference to Table 3,

analysis of variance of implantation counts - "...attributable to the second substance included in the test." This needs clarification. The individual data for each male over the 12 mating periods indicate that all males successfully fertilized females at one or more intervals with some having a better success rate than others. No male appeared to be sterile.
JR(G), 3/6/85

026 016821, "Ss 2074, Chinomethionate (ISO), Oxythioquinox (BSI), Morestan active ingredient; Micronucleus Test on the Mouse to Evaluate for Mutagenic Effect." (Bayer AG, Institute of Toxicology, 2/5/82, Report No. 10616, also No. 80617) Ss 2074 (oxythioquinox), batch 9030173, 95.2%; 5/sex/group were given 0, 500 or 1000 mg/kg by oral gavage, two doses; sacrificed at 6 hours after the second dosing; dose selection based on preliminary test at 2 x 500, 2 x 1000 mg/kg; no adverse clinical signs reported in the actual test at the higher dose; 1000 polychromatic erythrocytes scored per animal and the number of normochromatic erythrocytes per 1000 PCE's reported. No increase in micronuclei indicated. UNACCEPTABLE (single sacrifice time, inadequate high dose). JR(G), 3/8/85

MUTAGENICITY, DNA/OTHER

032 016816, "Report of Mutagenicity Test on Bacteria." (Nitokuno, 11/5/75) A series of compounds including Morestan were assayed with Bacillus subtilis strains NIG 45 and NIG 17. Morestan at 300 ug/disk with a "-" reported - no data. JR(G), 3/8/85

038 036708, "Chinomethionat (Morestan) Mutagenicity Test on Bacterial Systems." (Institute of Environmental Toxicology, 11/26/79, Report No. 89030) Morestan, 91%, tested with Bacillus subtilis strains H17 and M45 in rec assay by disk method; without activation only; tested at 0, 20, 50, 100, 200, 500, 1000 or 2000 ug/disk, single plate; no difference in growth between strains and no evidence of cytotoxicity = no test; UNACCEPTABLE (activation not included, no effect on growth of either strain.) JR(G), 12/27/85.

**051 060684, "Unscheduled DNA Synthesis in Rat Primary Hepatocytes." (Microbiological Associates, 10/27/86, Report 94409 of Mobay) Morestan technical, 94.4%; tested with primary hepatocytes from a male Sprague-Dawley rat at 0 (DMSO vehicle control and medium control), 0.01, 0.03, 0.1, 0.3, 1.0 and 3.0 µg/ml, 18 - 20 hours, triplicate cultures; ³H-thymidine for labelling followed by autoradiography; scored 25 nuclei from each of 3 slides for a total of 75 nuclei per concentration; 3.0 µg/ml was too toxic to score; no evidence for unscheduled DNA synthesis; ACCEPTABLE. Gee, 7/21/88.

NEUROTOXICITY

Not required at this time.

023 31938, "Neurotoxicity to Chickens." (Bayer, 12/14/62, Report No. 12161) Ss2074, oxythioquinox, Batch 124, given in a single oral dose to chickens at 0.50, 0.25 or 0.20 g/kg or i.p. at 0.15, 0.075 or 0.05 g/kg; 6 weeks of observation; number per group is not clear but appears to be 10 to 15; lethality but no neurotoxic effects detected; UNACCEPTABLE (one page summary). JR(G), 3/6/85.